

Cb
contd.

of said microcapsules, and further wherein both the first and second melting points are lower than the Curie point of the magnetic particles.

Please cancel without prejudice claims 3 and 46.

REMARKS

Claims 1-59 and 69-71 are pending in the instant application. Claims 1-59 and 69-71 have been rejected. Claims 1, 4, 41, 44, 47 and 69 have been amended. Claims 3 and 46 have been canceled. No new matter has been added by these amendments to the claims. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Rejection of Claims Under 35 U.S.C. § 102

A. Rejection Over Unger et al. (US Patent 5,853,752)

Applicant's arguments with regard to the previous rejection of claims 1-59 and 69-71 under 35 U.S.C. 102(e) as being anticipated by Unger et al. (US Patent 5,853,752; hereinafter referred to as Unger) were considered not persuasive by the Examiner and the rejection was maintained. The Examiner suggests that independent claim 1 recites a limitation for the function of an energy absorbing component, which does not cause a structural difference between the claimed invention and the prior art. The Examiner goes on to suggest that the instant claims use the open-ended comprising language leaving them to be read with their broadest reasonable interpretation. Applicants respectfully traverse this rejection.

Applicants again respectfully point out that Unger does not teach the encapsulation of an energy absorbing component that is specifically heated to a temperature beyond the melting point of the outer membrane by the absorption of energy. Unger teaches that metal ions can be complexed to lipid head groups that increase the rate of formation of reactive oxygen intermediates when exposed to thermal

irradiation, which describes a structurally different method for disruption of the membrane than the instant claims. Independent claim 1 states that one or more energy absorbing components in an internal liquid phase is in contact with the outer membrane, not complexed with lipid groups. As argued earlier, being in contact and being complexed with a membrane are two very different states and the teaching of Unger would not lead one of ordinary skill to assume that they are interchangeable. In addition, claim 1 was amended in the previous response to recite “wherein the temperature of said energy absorbing component is increased by absorbing said energy to melt at least a portion of the polymer membrane.” Therefore, the energy absorbing component is specifically heated to melt a portion of the polymer membrane, something that is not taught by Unger et al.

Further, as discussed in the previous response, independent claims 1, 41, 44 and 69 each contain limitations related to temperature, none of which are taught or suggested by Unger et al. Claim 1 was amended to recite “wherein the temperature of said energy absorbing component is increased by absorbing said energy to melt at least a portion of the polymer membrane.” Claim 41 recites at least two groups of microcapsules, each group containing a magnetic particle with a Curie point that is different from the Curie point of the magnetic point in the other group and where the Curie point of all magnetic particles is higher than the melting temperature of the polymer membrane. Claim 44 recites “exposing the microcapsules to an energy source, effective to heat the internal component and to melt at least a portion of the polymer outer membrane and to release the drug.” Amended claim 69 recites at least two groups of microcapsules, each having an outer membrane with a different melting point and where each melting point is less than the Curie point of the magnetic particles.

As stated earlier, to anticipate a claim, the prior art reference must teach each and every claim limitation. The prior art reference of Unger et al. fails to teach each and every claim limitation as discussed above and thus cannot anticipate the claims. However, in an earnest effort to advance the prosecution and facilitate allowance of the claims, Applicants have amended independent claims 1, 41, 44

and 69 to include the language “consisting of” in order to more clearly define the instant invention. Using this language, the microcapsules and the methods of the instant invention clearly are not anticipated by Unger et al. Accordingly, withdrawal of this rejection is respectfully requested.

B. Rejection Over Grinstaff et al. (US Patent 5,498,421)

The rejection of claims 1-43 and 69-71 under 35 U.S.C. 102(b) as being anticipated by Grinstaff et al. (US Patent 5,498,421; hereafter referred to as Grinstaff) was maintained as the Examiner suggested Applicants arguments were found not to be persuasive. Specifically, the Examiner suggests that Grinstaff teaches a polymeric shell for delivery of biologicals comprising an outer polymer membrane, an energy absorbing component such as metal particles selected from the group consisting of iron, iron oxide, and manganese, a biocompatible dispersing agent such as soybean oil, corn oil, cotton seed oil, and a drug selected from various therapeutic classes in a pharmaceutically acceptable carrier. The Examiner goes on to suggest that the mere recitation of “energy absorbing component” in the instant claims does not exclude all the components that are described in the prior art which possess that property. Applicants respectfully traverse this rejection.

Grinstaff teaches compositions for delivery of biologicals that are composed of an outer polymer membrane made of a biocompatible material. Nowhere, however, does this patent teach or suggest the limitations of the claims of the instant invention which are a microcapsule where energy absorbing components such as graphite, aluminum powder or TWEEN are in contact with the outer membrane and where the property of the energy absorbing component is used to melt a portion of the polymer membrane as the method of drug delivery. However, in an earnest effort to advance the prosecution, Applicants have amended the claims to limit the group of energy absorbing components to those specifically mentioned in the instant specification and which are not taught by Grinstaff. Accordingly, this prior art patent does not anticipate the amended claims and withdrawal of this rejection is respectfully requested.

C. Rejection of Claims Over McGinity et al. (US Patent 5,288,502)

The rejection of claims 1, 3-9, 11, 21-23, 31-35, and 40-43 under 35 U.S.C. 102(b) as being anticipated by McGinity et al. (US Patent 5,288,502; hereafter referred to as McGinity) was maintained. Specifically, the Examiner suggests that McGinity discloses microspheres that comprise two immiscible liquid phases comprising Tween 80 and that since the instant specification recognizes Tween 80 as an energy absorbing material it would possess energy absorbing qualities and have the same characteristics of the instant microcapsules. With the exception of cancelled claim 3, Applicants respectfully traverse this rejection of the claims.

At the outset, as discussed above, Applicants have amended the claims of the instant invention to more specifically define the microcapsules through use of the “consisting of” language. This language defines the instant invention as distinct from the teachings of McGinity. This is because, as discussed in the previous Office Action response, McGinity does not teach the use of an external energy source to heat an energy absorbing compound to melt a hole in the outer polymer membrane. McGinity describes polymeric microspheres with a molecular compound in microemulsions dispersed throughout a polymer matrix. A biodegradable polymer surrounds a fixed oil or oil/aqueous emulsion containing a water-soluble or insoluble drug; see column 3, lines 61-67. The method of drug delivery is biological degradation of the polymer for a slow release of the drug-containing microemulsions; see column 9, lines 11-14 and column 12, lines 55-68. McGinity does not describe at all the use of an energy absorbing compound that is specifically heated to melt a hole in an outer polymer membrane to disrupt the microsphere. Therefore, McGinity fails to teach each and every limitation of the instant claims as amended and cannot anticipate the instant invention. Accordingly, withdrawal of this rejection is respectfully requested.

D. Rejection of Claims Over Tsuei et al. (US patent 5,589,194)

The rejection of claims 1-4, 6-8, 21, 24, 26-27, 36, 40-44, and 69-71 under 35 U.S.C. 102(b) as being anticipated by Tsuei et al. (US Patent 5,589,194; hereafter referred to as Tsuei) was maintained. Specifically, the Examiner suggests that the different functionality of individual components of the instant invention does not impart patentability because the invention as a whole comprises the same characteristics as those of Tsuei. With the exception of cancelled claim 3, Applicants respectfully traverse this rejection.

As discussed in the previous response, Tsuei does not teach microcapsules with an outer polymer membrane, surrounding one or more internal immiscible liquid phases as claimed in the instant invention. In column 2, lines 26-33, Tsuei describes the creation of a solid phase in which the active component is dissolved; the solution is then injected into a quenching liquid to solidify the material into microspheres. Further, Tsuei does not teach the use of an energy absorbing component that is specifically heated to melt a hole in a portion of the outer polymer membrane. Tsuei describes the use of filler components such as graphite to be used to reduce the cost of the matrix, to modify the active component, or to slow the release process of the component by providing a block to diffusion; see column 5, lines 28-37. Additional components, such as magnetic particles or energy absorbing particles, are described that can be incorporated at the outer surface of the microcapsule (column 6, lines 50-57) and can aid in melting of the solid matrix on direct heating (column 10, lines 20-25). However, these particles at the outer surface are described as aiding the melting of the entire outer surface of the solid matrix at once. Tsuei does not describe the use of an energy absorbing particle that is specifically heated to melt a hole in a portion of the outer polymer membrane as claimed in the instant invention; further, Tsuei does not describe the use of an outer polymer membrane at all. However, Applicants have amended the claims to use language that more distinctly defines the instant invention, as discussed above. Accordingly, the claims as amended are not anticipated by Tsuei because this reference does not teach or suggest the limitations of

the instant invention of the amended claims. Accordingly, withdrawal of this rejection is respectfully requested.

II. Rejection of Claims Under 35 U.S.C. § 103(a)

The rejection of claims 1-59 and 69-71 were rejected under 35 U.S.C. 103(a) as being unpatentable over Tsuei et al. (US Patent 5,589,194) and Unger et al. (US Patent 5,853,752) was maintained. The Examiner found the arguments presented by the Applicant in the previous response to be not persuasive and continues to suggest it would have been *prima facie* obvious for one of ordinary skill in the art to develop a microcapsule comprising various types of pharmaceutical agents as taught by Unger et al. to create microcapsules that by methods taught by both Tsuei and Unger, and although Tsuei does not specifically teach methods utilizing various energy sources they suggest use of an external energy source for releasing active drug from the microcapsules and it would have been obvious to one of ordinary skill to apply various energy sources as taught by Unger et al. Applicants respectfully traverse this rejection.

As discussed *supra* in Section I, Applicants have amended the claims to more clearly distinguish the instant invention from the prior art. Also as discussed in Section I, each of these primary references cited by the Examiner fails to teach the instant invention and all of its limitations as claimed. Unger does not teach the encapsulation of an energy absorbing component that is specifically heated to a temperature beyond the melting point of the outer membrane by the absorption of energy. The claims of the instant invention recite a “wherein the temperature of said energy absorbing component is increased by absorbing said energy to melt at least a portion of the polymer membrane.” Therefore, the energy absorbing component is specifically heated to melt a portion of the polymer membrane, something that is not taught by Unger et al.. Rather than encapsulating an energy absorbing component to control the heating of a component to melt the outer membrane, Unger teaches the coordination of membrane composition with

peak resonant frequency of a gaseous precursor to rupture the liposomes. Also as discussed *supra* in Section I, Tsuei et al. fail to teach the limitations of the invention as claimed. Tsuei does not teach microcapsules with an outer polymer membrane, surrounding one or more internal immiscible liquid phases as claimed, nor use of an energy absorbing component that is specifically heated to melt a hole in a portion of the outer polymer membrane. In fact, Tsuei et al. teaches microcapsules that are a solid phase with an active component dissolved in that solid phase, which is very different than the microcapsules of the instant invention.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. Clearly, the combination of prior art cited fails to teach or suggest the limitations of the claims as now amended as not one of the cited references, either alone or in combination, teaches or suggests microcapsules that specifically consist of an outer polymer membrane, surrounding one or more internal immiscible liquid phases and use of energy absorbing components to melt a portion of the outer membrane and release an active component contained in the internal phases. Therefore, the cited references would not motivate one to make the microcapsules of the instant invention and cannot render the instant claimed invention obvious. Therefore, withdrawal of this rejection is respectfully requested.

III. Conclusions

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited. If the Examiner has any questions or suggestions concerning the application or

allowance of any claim thereof, or feels that an interview would advance the examination process, the Examiner is requested to call the Applicants' undersigned attorney at the direct dial number printed below.

Respectfully,



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